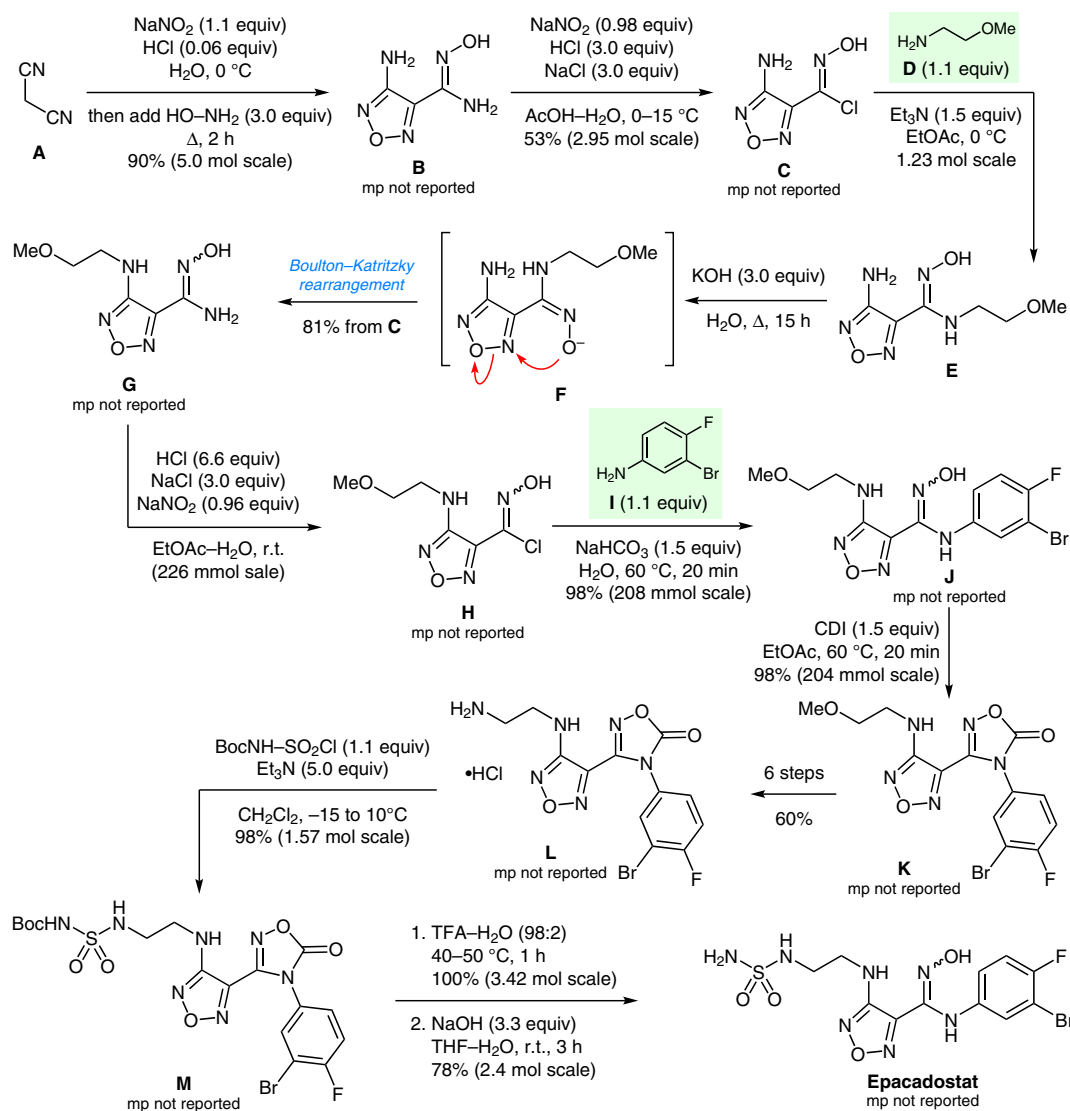


Synthesis of Epacadostat



Significance: Epacadostat (INCB24360) inhibits the immunomodulatory activity of indoleamine-2,3-dioxygenase 1, thereby making possible the restoration and/or activation of the immune system in cancer therapy. In combination with pembrolizumab, epacadostat is currently in a phase III clinical trial for the treatment of metastatic melanoma.

Comment: Synthesis of the secondary 3-amino-furazan **G** by direct alkylation or reductive amination of the primary 3-amino substituent in **E** was low yielding, presumably due to the electron deficiency of the furazan. A general and robust alternate route to secondary amino-furazan **G** was accomplished through a Boultou-Katritzky rearrangement of the amidooxime furazan **E**.